UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,522	11/28/2001	Roger Coleman	PF-0041-4 CON	5024

27904 7590 09/03/2002

INCYTE GENOMICS, INC.
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/03/2002

6

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,522	COLEMAN ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,9,10,12-16,28,29,46,47 and 56-58* is/are pending in the application.

4a) Of the above claim(s) *1,14-16,28,29,46,47 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7,9,10,12,13,57 and 58* is/are rejected.

7)☒ Claim(s) *4,5,10 and 57* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1.5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparisons A and B* .

DETAILED ACTION

1. Formal Matters

A. Amendment B, filed 6/13/02, has been entered into the record.

B. Preliminary Amendment A, filed 11/28/01, has been entered into the record.

C. The Information Disclosure Statement, filed 11/28/01, has been entered into the record.

D. Claims 1-57 were pending. Claims 2, 8, 17-27, 30-45 and 48-55 were cancelled in Preliminary Amendment A, filed 11/28/01. Claims 1, 3-7, 9-16, 28, 29, 46, 47, 56 and 57 were subject to restriction in Paper No. 4, dated 5/9/02. In Paper No. 5, filed 6/13/02, Applicants elected Group II, claims 3-7, 9, 10, 12, 13 and 57, with traverse. Applicants argue that methods of using the claimed polynucleotides could and should be examined together with the product claims from which they depend. Applicants, therefore, presume that these method claims will be rejoined upon determining allowability of the product claims from which they depend. These dependent method claims will be rejoined if the product claims are found allowable and if the method claims are commensurate in scope with the elected invention and do not raise any new issues under 35 USC 112. This restriction is deemed proper and is, therefore, made FINAL. In addition, Paper No. 5 (Amendment B) also cancelled claim 11 and added new claim 58. The Examiner has included claim 58 into elected Group II. Therefore, claims 1, 14-16, 28, 29, 46, 47 and 56 are withdrawn as being drawn to a non-elected invention and claims 3-7, 9, 10, 12, 13, 57 and 58 are the subject of this Office Action.

E. Though not the basis of a rejection or an objection, the syntax of claim 9 could be improved by replacing the preamble and part (a) of the claim with the following:

"A method of producing a polypeptide, said method comprising:
(a) culturing the cell of claim 7 under conditions in which the polypeptide is expressed; and"

2. Information Disclosure Statement

A. Reference 10 on the IDS, filed 11/28/01, has been lined thru since the publication date has not been cited in the reference.

3. Claim Objections

A. If the present invention was shown to possess utility under 35 USC 101, claims 4, 5, 10 and 57 would be objected to since they depend from claims 3, 9 and 12, which would be rejected under 35 USC 112, first paragraph, as recited in the scope of enablement rejection below.

B. Claims 4, 5, 10 and 57 are objected to since they depend from claims 3, 9 and 12, which are rejected under 35 USC 112, first paragraph, as recited in the written description rejection below.

C. Claim 5 is objected to since the phrase "an isolated" should be replaced with the phrase "the isolated."

4. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 3-7, 9, 10, 12, 13, 57 and 58 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well-established utility. These claims are directed to an isolated polynucleotide of SEQ ID NO:1 which encodes a thrombin receptor of SEQ ID NO:2, or fragments thereof, as well as transformed cells and methods for making this protein. However, the invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines, published 1/5/01, 66 FR 1092. The instant application has provided a description of an isolated polynucleotide encoding a protein. However, the instant application does not disclose a specific and substantial biological role of this protein or its significance.

It is clear from the instant specification that the claimed receptor is what is termed an "orphan receptor" in the art. The instant application does not disclose the biological role of the protein encoded for by the claimed polynucleotide, or its significance. Applicants disclose in the specification that this receptor is believed to be a thrombin receptor. However, the basis that the receptor encoded for by the polynucleotide of the present invention is only known to be homologous to thrombin receptors (page 2, lines 21-26 of the specification) is not predictive of a use. There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further

characterization, however, is part of the act of invention and, until it has been undertaken, Applicants' claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The specification discloses that the polynucleotide of the invention encodes a protein which has significant sequence similarity to two different receptors - a known human thrombin receptor and only partial homology to a platelet activating receptor (page 2, lines 21-26 of the specification). Based on the structural similarity, the specification asserts that the newly disclosed SEQ ID NO:1 and 2 have similar activities to the thrombin receptor (page 5, lines 20-21). The assertion that the disclosed proteins have biological activities similar to known thrombin receptors cannot be accepted in the absence of supporting evidence, because generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases.

For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not

necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the claimed polynucleotide of SEQ ID NO:1 which encodes the protein of SEQ ID NO:2, which is only known to be homologous to thrombin receptors. Therefore, the instant claims are drawn to a polynucleotide encoding a protein which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said protein identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for said protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Furthermore, since the nucleic acid (SEQ ID NO:1) and protein (SEQ ID NO:2) of the invention are not supported by a specific and substantial asserted utility or a well established utility, the host cell, method for producing the protein, the polynucleotide encoding thrombin-binding and immunogenic fragments as well as naturally occurring variants of said sequences and polynucleotides comprising at least 60 contiguous bases of SEQ ID NO:1, or of said variants also lack utility.

5. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 3-7, 9, 10, 12, 13, 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

6. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Furthermore, even if the invention possessed utility under 35 USC 101, claims 3, 6, 7, 9, 12, 13 and 58 would be rejected under 35 U.S.C. 112, first paragraph, because the specification, while then being enabling for SEQ ID NO:1 and 2, does not reasonably provide enablement for polynucleotides encoding thrombin-binding fragments of SEQ ID NO:2, naturally occurring human variants of SEQ ID NO:1 or 2, or at least 60 contiguous nucleotides of a naturally occurring human variants of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all polynucleotides which are "**naturally occurring human variants**" of SEQ ID NO:1. Polynucleotides which encode proteins which are naturally occurring human variants of SEQ ID NO:2, or are "**at least 60 contiguous nucleotides**" of a naturally occurring human variants of SEQ ID NO:1, would have one or more nucleic acid substitutions, deletions, insertions and/or additions to SEQ ID NO:1 and these proteins would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:2. Similarly, "**thrombin-binding fragments**" of SEQ ID NO:2 would also have one or more amino acid deletions to SEQ ID NO:2.

Applicants provide no guidance or working examples of polynucleotides which are "naturally occurring human variants" of SEQ ID NO:1, or which encode SEQ ID NO:2, nor do they provide a *function* of these variants. Similarly, Applicants do not provide any guidance or working examples of thrombin-binding fragments. Applicants have not taught the artisan how to identify a naturally occurring human variant of SEQ ID NO:1 or 2, or what critical residues are necessary to maintain the function of a variant of this protein, or how to determine whether or not a protein, or its encoding polynucleotide, is considered a naturally occurring human variant, nor do they teach what residues are required in order to maintain the thrombin-binding characteristics of SEQ ID NO:2. No residues necessary for the binding of thrombin to SEQ ID NO:2 have been identified. Furthermore, it is not predictable to one of ordinary skill in the art how to identify a naturally occurring human variant of SEQ ID NO:1 or 2, or what critical residues are necessary to maintain the function of a variant of SEQ ID NO:2, or to determine whether or not a protein, or its encoding polynucleotide, is considered a naturally occurring human variant, nor is it predictable to the artisan what residues are required to maintain the thrombin-binding characteristics of SEQ ID NO:2.

Furthermore, the claims include in scope allelic variants of the disclosed thrombin molecules. The Examiner notes, though allelic variants are not specifically defined in the specification, the phrase "naturally occurring TRH," which is defined on page 5 of the specification as "...TRHs produced by human cells that have not been genetically engineered...", reads on allelic variants. The Examiner cannot determine how one would distinguish, merely by examination of the protein, whether a protein were the result of expression of a different allele, or alternatively, were merely one of a number of ultimate species that might be obtained by the expression of SEQ ID NO:1 disclosed in this application. Enablement is not commensurate in scope with claims to proteins potentially encoded for by allelic variants of SEQ ID NO:1, or those of SEQ ID NO:2. Allelic variants often encode proteins with quantitatively or qualitatively altered or absent biological activity. Therefore, the specification does not teach how to use such variants, nor is adequate guidance provided for the skilled artisan to predict, *a priori*, which variants would reasonably be expected to retain biological function.

In summary, the breadth of the claims is excessive with regard to claiming all polynucleotides which are "naturally occurring human variants" of SEQ ID NO:1, those which encode SEQ ID NO:2, or those which comprise at least 60 contiguous bases thereof. There is also a lack of guidance and working examples of these nucleic acid molecules and proteins as well as a lack of guidance, working examples and predictability how to identify a naturally occurring human variant of SEQ ID NO:1 or 2, or what critical residues are necessary to maintain the function of this variant protein or of a thrombin-binding

fragment of SEQ ID NO:2, or to determine whether or not a protein, or its encoding polynucleotide, is considered a naturally occurring human variant. For this reason, the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

7. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 3, 6, 7, 9, 12, 13 and 58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Polynucleotides which are, or which encode, naturally occurring human variants of SEQ ID NO:1 or 2, or polynucleotides of at least 60 contiguous bases thereof, would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the polynucleotide of SEQ ID NO:1, or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:2. Similarly, thrombin-binding fragments of SEQ ID NO:2 would also have one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:2.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes are made to SEQ ID NO:1 or 2 to be considered a naturally occurring human variant, or what residues of SEQ ID NO:2 constitute a thrombin-binding fragment. Structural features that could distinguish compounds in the genus from others in the polynucleotide or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1 and 2 alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

B. Claims 3, 6, 7, 9, 12, 13 and 58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:1 and 2 and equivalent degenerative sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to naturally occurring human variants of SEQ ID NO:1 and 2.

Claims 3, 6, 7, 9, 12, 13 and 58 are drawn to the genus including all DNA alleles of SEQ ID NO:1 which encode SEQ ID NO:2 and its variants. The Examiner notes, though allelic variants are not specifically defined in the specification, the phrase "naturally occurring TRH," which is defined on page 5 of the specification as "...TRHs produced by human cells that have not been genetically engineered...", reads on allelic variants. The structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:1 and 2, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and polypeptides and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polynucleotide or protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

The specification discloses only one allele encoding the protein within the scope of the genus: SEQ ID NO:1 for the protein of SEQ ID NO:2. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of the DNA encoding the claimed variants relates to the structure of different alleles. In addition, according to the standard definition, the genus includes members that would be expected to have widely divergent functional properties. The general knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is representative of other unknown alleles having concordant or discordant functions. The common attributes of the genus are not described and the identifying attributes of individual alleles, other than SEQ ID NO:1, or the protein of SEQ ID NO:2, are not described. The nature of alleles is that they are variant structures where the structure of one does not provide guidance to the structure and function of others. According to these facts, one of skill in the art would conclude that the Applicant was not in possession of the claimed genus because a description of only one member of the genus is not representative of the variants of the genus and is insufficient to support the claim.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with

reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention." This is insufficient to support the generic claims as provided by the Interim Written Description Guildlines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore only an isolated DNA molecule comprising a DNA sequence consisting of SEQ ID NO:1 and 2 and equivalent degenerative codon sequences thereof, as well as SEQ ID NO:2, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

8. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 3, 6, 7 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 is confusing since it is not clear in part (c) whether the fragment is a fragment of SEQ ID NO:2, or if the fragment comprises SEQ ID NO:2 wherein SEQ ID NO:2 is part of a larger protein. If the intent is that the fragment is a part of SEQ ID NO:2, part (c) can be rewritten as "a thrombin-binding fragment of SEQ ID NO:2." Claims 6, 7 and 9 are rejected since they depend from rejected claim 3.

9. Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

A. Claim 4 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 5,686,597. This is a double patenting rejection. Claim 4 of the present application recites an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2. Claim 1 of the patent recites an isolated polynucleotide encoding a thrombin receptor homolog of SEQ ID NO:2. Though claim 4 of the application does not recite "thrombin receptor homolog," since the sequences are 100% identical, the protein of the present invention would inherently encode a thrombin receptor. Therefore, one of ordinary skill in the art would immediately envision that the encoded proteins of both the patent and application are the same.

B. Claims 5 and 57 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 3 of prior U.S. Patent No. 5,686,597. This is a double patenting rejection. Claims 5 and 57 of the present application recite an isolated polynucleotide comprising the polynucleotide sequence of SEQ ID NO:1. Claim 3 of the patent recites a recombinant DNA molecule comprising SEQ ID NO:1. Though neither claims 5 nor 57 of the application recite that the polynucleotide is "recombinant," one of ordinary skill in the art would not be able to differentiate a "recombinant" polynucleotide from a "non-recombinant" polynucleotide since they would have the same inherent structure. Therefore, one of ordinary skill in the art would immediately envision the that the polynucleotides of claims 5 and 57 of the application could be recombinant and, therefore, identical to that of claim 3 of the patent.

10. Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

A. Claims 3, 4, 5, 12, 13 and 57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,869,633. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 3 and claim 4 of the present application recite an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2. Claim 5 of the present application recites an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2 wherein the polynucleotide is SEQ ID NO:1. Claim 12 recites a polynucleotide comprising SEQ ID NO:1. Claim 13 recites a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:1. Claim 57 recites the polynucleotide of SEQ ID NO:1. Claim 1 of the patent recites an isolated polynucleotide complementary to a polynucleotide encoding the polypeptide of SEQ ID NO:2. SEQ ID NO:2, as recited in the patent, is encoded for by SEQ ID NO:1, as recited in the application (see the specific disclosure in column 4, lines 21-26 of the patent). Though the claims of the application do not recite "thrombin receptor homolog," since SEQ ID NO:1 and 2 are 100% identical in both the patent and application, the protein of the present invention would inherently encode a thrombin receptor. Therefore, one of ordinary skill in the art would immediately envision that the encoded proteins of both the patent and application are the same. Given the claimed complement (i.e. antisense) of a polynucleotide encoding SEQ ID NO:2, as recited in the patent, one of ordinary skill in the art would immediately envision the sense strand to this polynucleotide, which would encode SEQ ID NO:2 and which includes that of SEQ ID NO:1 of the present application. In addition, the sense strand of a polynucleotide encoding SEQ ID NO:2, as recited in the patent, would encode a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID

NO:1, as recited in the application, especially given that the claim of the patent does not recite that the complement is "fully complementary."

Given that it was known that SEQ ID NO:1 encodes SEQ ID NO:2, it would have been obvious for one of ordinary skill in the art to have obtained the sense strand to a complement of a polynucleotide encoding SEQ ID NO:2, including SEQ ID NO:1 since, not only is this the strand which encodes for a protein, but the sense strand would be required in order for the artisan to produce recombinant expression vectors, host cells and the protein of interest since the antisense strand, alone, would not be able to produce the protein of interest. The artisan would have been motivated to produce the sense strand to the complement recited in the patent in order to amplify the polynucleotide and to produce the encoded protein for binding and functional assays in order to identify compounds which can be used in the treatment of human diseases involving this protein. There would have been a high expectation of success in obtaining this sense strand to the complement of the patent since DNA cloning and amplification techniques were well-known and highly successful in the art at the time of the present invention.

Similarly, it would have been obvious for one of ordinary skill in the art to make a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:1 to use as a hybridization probe to identify DNA encoding homologous receptors, or for tissue typing or chromosomal localization. This information would help to further characterize the polynucleotide and protein of the present invention and help to further elucidate molecular mechanisms of these molecules in an organism. There would have been a high expectation of success in producing and using these polynucleotides since DNA cloning, amplification and hybridization techniques were well-known and highly successful in the art at the time of the present invention.

B. Claims 3, 12 and 13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 5,686,597. Claim 4 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of U.S. Patent No. 5,686,597. Claims 5 and 57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,686,597. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 3 and 4 of the present application recite an isolated polynucleotide encoding the protein of SEQ ID NO:2, which reads on claim 3 of the patent since claim 3 recites a recombinant DNA comprising SEQ ID NO:1. SEQ ID NO:1 encodes SEQ ID NO:2.

Claim 5 of the present application recites an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2 wherein the polynucleotide is SEQ ID NO:1, and claims 12 and 57 recites the polynucleotide of SEQ ID NO:1, both of these claims read on claim 1 of the patent since claim 1 recites an isolated polynucleotide encoding a thrombin receptor homolog of SEQ ID NO:2. Claim 13 recites a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:1. Claim 1 of the patent recites an isolated polynucleotide encoding a thrombin receptor homolog comprising the amino acid sequence of SEQ ID NO:2. Claim 3 of the patent recites the polynucleotide of SEQ ID NO:1. Therefore, claim 3 of the patent would encode a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:1, as recited in the application.

Though the claims of the application do not recite "thrombin receptor homolog," since the sequences are 100% identical, the protein of the present invention would inherently encode a thrombin receptor. Therefore, one of ordinary skill in the art would immediately envision that the encoded proteins of both the patent and application are the same.

It would have been obvious for one of ordinary skill in the art to make a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:1 to use as a hybridization probe to identify DNA encoding homologous receptors, or for tissue typing or chromosomal localization. This information would help to further characterize the polynucleotide and protein of the present invention and help to further elucidate molecular mechanisms of these molecules in an organism. For these reasons it would have also been obvious to the artisan, given either SEQ ID NO:1 or 2, to obtain all DNA encoding SEQ ID NO:2 in order to have a complete record of all the polynucleotides which encode SEQ ID NO:2 which will aid in understanding of the differences in these polynucleotides and potential mutational sites which exist in these polynucleotides between individuals which are predisposed to disease. There would have been a high expectation of success in producing and using these polynucleotides since DNA cloning, amplification and hybridization techniques were well-known and highly successful in the art at the time of the present invention.

C. Claim 6 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of U.S. Patent No. 5,686,597. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 6 of the present application recites a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding SEQ ID NO:2. Claim 2 of the patent recites a polynucleotide encoding SEQ ID NO:2 further

comprising a control sequence. Though claim 6 of the application does not recite "thrombin receptor homolog," since the sequences are 100% identical, the protein of the present invention would inherently encode a thrombin receptor. Therefore, one of ordinary skill in the art would immediately envision that the encoded proteins of both the patent and application are the same. However, claim 6 of the application recites "promoter" and claim 2 of the patent recites "control sequence."

Though not all control sequences are promoters, it would have been obvious for one of ordinary skill in the art to have used a promoter for the control sequence of the patent in order to allow for the protein encoded for by the polynucleotide of the invention to be expressed. The artisan would have been motivated to use a promoter in order to not only aid in expression of the protein of interest, but to express this protein in a larger quantity than otherwise may be produced in the absence of a promoter in order to produce the encoded protein for binding and functional assays in order to identify compounds which can be used in the treatment of human diseases involving this protein. There would have been a high expectation of success in using a promoter along with the polynucleotide of the patent since DNA cloning and amplification techniques were well-known and highly successful in the art at the time of the present invention.

D. Claims 9 and 10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of U.S. Patent No. 5,686,597. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 9 and 10 of the present application recite a method of producing the polypeptide of SEQ ID NO:2. Claim 6 of the patent recites a method of producing the thrombin receptor homolog of SEQ ID NO:2. Though claims 9 and 10 of the application do not recite "thrombin receptor homolog," since the sequences are 100% identical, the protein of the present invention would inherently encode a thrombin receptor. Therefore, one of ordinary skill in the art would immediately envision that the encoded proteins of both the patent and application are the same. However, claims 9 and 10 of the application recite the use of a "promoter" and the patent recites the use of an "expression vector."

Though not all expression vectors require a promoter, it would have been obvious for one of ordinary skill in the art to have used a promoter in the expression vector of the patent in order to allow for the protein encoded for by the polynucleotide of the invention to be expressed. The artisan would have been motivated to use an expression vector with a promoter in order to not only express the protein of interest, but to express this protein in a larger quantity than otherwise may be produced in an expression vector without a promoter in order to produce the encoded protein for binding and functional assays in

order to identify compounds which can be used in the treatment of human diseases involving this protein. There would have been a high expectation of success in using expression vectors comprising promoters since DNA cloning and amplification techniques were well-known and highly successful in the art at the time of the present invention.

E. Claims 6 and 7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4 and 5, respectively, of U.S. Patent No. 5,686,597. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 6 of the present application recites a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding SEQ ID NO:2. Claim 7 of the application recites a cell transformed with the polynucleotide of claim 6. Claim 4 of the patent recites an expression vector comprising the polynucleotide of SEQ ID NO:1. Claim 5 of the patent recites a host cell comprising SEQ ID NO:1.

Though neither claims 4 or 5 of the patent recite that the polynucleotide is "recombinant," one of ordinary skill in the art would not be able to differentiate a "recombinant" polynucleotide from a "non-recombinant" polynucleotide since they would have the same inherent structure. Therefore, one of ordinary skill in the art would immediately envision the that the polynucleotides of claims 4 and 5 of the patent could be recombinant and, therefore, identical to the polynucleotide of claim 6 and 7 of the application. Though the claims of the application do not recite "thrombin receptor homolog," since the sequences are 100% identical, the protein of the present invention would inherently encode a thrombin receptor. Therefore, one of ordinary skill in the art would immediately envision that the encoded proteins of both the patent and application are the same. Similarly, claims 4 and 5 of the patent recite the use of an "expression vector" whereas the application recites the use of a "promoter."

Though not all expression vectors require a promoter, it would have been obvious for one of ordinary skill in the art to have used a promoter in the expression vector of the patent in order to allow for the protein encoded for by the polynucleotide of the invention to be expressed. The artisan would have been motivated to use an expression vector with a promoter in order to not only express the protein of interest, but to express this protein in a larger quantity than otherwise may be produced in an expression vector without a promoter in order to produce the encoded protein for binding and functional assays in order to identify compounds which can be used in the treatment of human diseases involving this protein. There would have been a high expectation of success in using expression systems comprising promoters since DNA cloning and amplification techniques were well-known and highly successful in the art at the time of the present invention.

11. Closest Art

A. The closest art to SEQ ID NO:1 and 2 is not prior art. Marchese et al. (Genomics 56:12-21, 1999) teach a polynucleotide which is 98.9% identical to SEQ ID NO:1 (Sequence Comparison A) and 97.3% identical to SEQ ID NO:2 (Sequence Comparison B). However, these publications were published after the effective filing date of the present application.

12. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
August 26, 2002